IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF
FARRIES ET AL.
APPLICATION NO: Not Yet Assigned
FILED: Herewith
FOR: DOWN-REGULATED RESISTANT C3 CONVERTASE

Assistant Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Sir:

Kindly enter the following preliminary amendment prior to calculating the filing fee for this application.

IN THE SPECIFICATION

At page 1, between lines 1 and 2, insert -- This is a divisional of U.S. Application No. 09/142,334, filed September 4, 1998, which is a 371 of International Application No. PCT/GB 97/00603, filed March 4, 1997.

Please insert the appended "Sequence Listing," comprising pages numbered 71-87, into the specification following page 70.

Please renumber pages 71, 72, 73, 74, 75, 76 and 77 of the specification to be pages 88, 89, 90, 91, 92, 93, and 94, respectively.

Please amend the specification as follows:

Page 22/4, line 4 from bottom, after "Figure 1" insert --(SEQ. ID. NO: 22) --.

Page 22/4, line 3 from bottom, delete "Appendix 1 " and insert therefor --FIGURE 2 (SEQ. ID NO: 23) --.

Page 24, line 30, before the word "that", insert --(SEQ. ID. NO: 1) --.

Page 26, line 18, before the comma, insert --(SEQ.ID. NO: 2) --.

Page 26, line 19, before the comma, insert --(SEQ. ID. NO: 3) --.

Page 26, line 20, before the comma, insert --(SEQ ID. NO: 4) --.

Page 26, line 22, before the comma, insert --(SEQ. ID. NO: 5)

Page 26, line 23, before the word "and", insert --(SEQ. ID. N 0: 6) --.

Page 26, line 24, before the period, insert --(SEQ. I D. NO: 7) --.

Page 28, line 5, before the comma, insert --(SEQ. ID. NO: 24) --.

Page 36, line 18, before ..(letters", insert --(SEQ. ID. NO: 8) --.

Page 36, line 24, before the word "and", insert --(SEQ. ID. NO: 9) --,

Page 36, line 25, before the period, insert --(SEQ. ID. NO: 10) --.

Page 45, line 9, before the period, insert --(SEQ. ID. NO: 11) --.

Page 50, line 5, before the period, insert --(SEQ. ID. NO: 12) --.

Page 62/2, line 6, before the word "encoding", insert --(SEQ. ID. NO: 14) --.

Page 62/2, line 9, before the left parenthesis, insert --(SEQ. ID. NO: 15) --.

Page 62/2, line 11, before the left parenthesis, insert --(SEQ. ID. NO: 7) --.

Page 65/1, line 5, before the word ."encoding", insert --(SEQ. ID. NO: 18) --.

Page 67/1, line 9 under the subtitle, "2. Method", before the word "after", insert --(SEQ.ID. NO: 25) --.

Page 67/1, line 10 under the subtitle, ."2. Method", and before the word ."at", insert --(SEQ, ID. NO: 26) --

Page 68/3, line 4 under the subtitle, ."2. Method", and before the word ."encoding", insert --(SEQ. ID. NO: 19) --.

Page 68/3, line 6 under the subtitle, "2. Method", and before the word "encoding", insert --(SEQ. ID. NO: 20) --.

Page 68/8, third line in column entitled ."Sequence replaced", i.e. after "LSSDFWGE", insert --(SEQ. ID. NO: 27) --.

Page 68/8, fourth line in column entitled "Sequence replaced", i.e. after ."IIGKD", insert -- (SEQ. ID. NO: 29) --.

Page 68/8, sixth line in column entitled "Sequence replaced", i.e. after '.EEDE", insert -- (SEQ. ID. NO: 31) --.

Page 68/8, seventh line in column entitled ."Sequence replaced", i.e. after .'QDEENQKQ", insert --(SEQ. ID. NO: 33) --.

Page 68/8, eighth line in column entitled "Sequence replaced", i.e. after "QDEENQKQ", insert --(SEQ. ID. NO:33) --.

Page 68/8, third line in column entitled .'Replaced by", i.e. after "KEALQI", insert --(SEQ. D. NO: 28) --.

Page 68/8, fourth line in column entitled .'Replaced by", i.e. after "RYIYPLDSL", insert --(SEQ. ID. NO: 30) --.

Page 68/8, sixth line in column entitled "Replaced by", i.e. after "RDTT", insert --(SEQ. ID. NO: 32) --.

Page 68/8, eighth line in column entitled "Replaced by", i.e. after "RSTRQRAA", insert --:SEQ. ID. NO: 34) --.

Page 68/8, ninth line in column entitled "Replaced by", i.e. after "AFLAN", insert --(SEQ. ID. NO: 35) --.

IN THE CLAIMS

Please cancel claims 2-36 and 38-50.

Please add the following new claims:

-- 51. (New) A method of reducing levels of complement pathway protein in a mammal comprising administering an effective amount of a modified human C3 protein which is capable of forming a stable C3 convertase wherein said modified protein is selected from the group consisting of:

(a) a C3 protein comprising one or more mutations in the region defined by amino acid residues 992-1005 of native human C3 (SEQ. ID. NO:22), whereby the C3b and C3I products, or their derived C3 convertases, are resistant to the complement inhibitory activity of Factor H;

(b) a C3 protein comprising one or more mutations in the region defined by amino acid residues 1546-1663 of native human C3 (SEQ. ID. NO:22), said protein having reduced susceptibility to Factor H and/or Factor I, relative to native human C3;

(c) a C3 protein comprising one or more mutations at amino acid residues 954 and/or 955 of native human C3 (SEQ. ID. NO:22), said protein having reduced susceptibility to cofactor-dependent Factor I-mediated cleavage at this position; and

(d) a C3 protein comprising mutations in native human C3 (SEQ. ID. NO:22) selected from any combination of the mutations specified in (a), (b), and (c).

52. (New) A method of treating transplant rejection in a mammal comprising administering an effective amount of a modified human C3 protein which is capable of forming a stable C3 convertase wherein said modified protein is selected from the group consisting of:

(a) a C3 protein comprising one or more mutations in the region defined by amino acid residues 992-1005 of native human C3 (SEQ. ID. NO:22), whereby the C3b and C3I products, or their derived C3 convertases, are resistant to the complement inhibitory activity of Factor H;

(b) a C3 protein comprising one or more mutations in the region defined by amino acid residues 1546-1663 of native human C3 (SEQ. ID. NO:22), said protein having reduced susceptibility to Factor H and/or Factor I, relative to native human C3;

(c) a C3 protein comprising one or more mutations at amino acid residues 954 and/or 955 of native human C3 (SEQ. ID. NO:22), said protein having reduced susceptibility to cofactor-dependent Factor I-mediated cleavage at this position; and

(d) a C3 protein comprising mutations in native human C3 (SEQ. ID. NO:22) selected from any combination of the mutations specified in (a), (b), and (c).

53. (New) A method of localizing and/or amplifying endogenous complement protein conversion and deposition at a specific site comprising administering an effective amount of a modified human C3 protein which is capable of forming a stable C3 convertase wherein said modified protein is selected from the group consisting of:

(a) a C3 protein comprising one or more mutations in the region defined by amino acid residues 992-1005 of native human C3 (SEQ. ID. NO:22), whereby the C3b and C3I products, or their derived C3 convertases, are resistant to the complement inhibitory activity of Factor H;

(b) a C3 protein comprising one or more mutations in the region defined by amino acid residues 1546-1663 of native human C3 (SEQ. ID. NO:22), said protein having reduced susceptibility to Factor H and/or Factor I, relative to native human C3;

(c) a C3 protein comprising one or more mutations at amino acid residues 954 and/or 955 of native human C3 (SEQ. ID. NO:22), said protein having reduced susceptibility to cofactor-dependent Factor I-mediated cleavage at this position; and

(d) a C3 protein comprising mutations in native human C3 (SEQ. ID. NO:22) selected from any combination of the mutations specified in (a), (b), and (c).

54. (New) A method of reducing complement-mediated destruction or damage to transplanted tissue of organs, comprising administering an effective amount of a modified human C3 protein which is capable of forming a stable C3 convertase wherein said modified protein is selected from the group consisting of:

(a) a C3 protein comprising one or more mutations in the region defined by amino acid residues 992-1005 of native human C3 (SEQ. ID. NO:22), whereby the C3b and C3I products, or their derived C3 convertases, are resistant to the complement inhibitory activity of Factor H;

(b) a C3 protein comprising one or more mutations in the region defined by amino acid residues 1546-1663 of native human C3 (SEQ. ID. NO:22), said protein having reduced susceptibility to Factor H and/or Factor I, relative to native human C3;

(c) a C3 protein comprising one or more mutations at amino acid residues 954 and/or 955 of native human C3 (SEQ. ID. NO:22), said protein having reduced susceptibility to cofactor-dependent Factor I-mediated cleavage at this position; and

(d) a C3 protein comprising mutations in native human C3 (SEQ. ID. NO:22) selected from any combination of the mutations specified in (a), (b), and (c).

55. (New) A DNA sequence coding for a modified human C3 protein which is capable of forming a stable C3 convertase wherein said modified protein is selected from the group consisting of:

(a) a C3 protein comprising one or more mutations in the region defined by amino acid residues 992-1005 of native human C3 (SEQ. ID. NO:22), whereby the C3b and C3I products, or their derived C3 convertases, are resistant to the complement inhibitory activity of Factor H;

(b) a C3 protein comprising one or more mutations in the region defined by amino acid residues 1546-1663 of native human C3 (SEQ. ID. NO:22), said protein having reduced susceptibility to Factor H and/or Factor I, relative to native human C3;

(c) a C3 protein comprising one or more mutations at amino acid residues 954 and/or 955 of native human C3 (SEQ. ID. NO:22), said protein having reduced susceptibility to cofactor-dependent Factor I-mediated cleavage at this position; and

(d) a C3 protein comprising mutations in native human C3 (SEQ. ID. NO:22) selected from any combination of the mutations specified in (a), (b), and (c).

56. (New) A DNA construct (e.g. a vector) comprising a DNA sequence as defined in claim 51.

REMARKS

Early examination of the claims and allowance of the same are respectfully requested.

Respectfully submitted,

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